REMARKS

Claims 32, 34, 39, 41, 42, 45-47 and 56-64 are currently pending; claims 32, 34, 39, 41, 42, 45-47 and 56-58 being currently amended; and claims 61-64 being added by the present amendment.

Claim Amendments

Independent claims 32, 56 and 57 have been amended to recite that the solution comprises between 0% and 10% (v/v) ethanol and water. No change in scope is intended by this amendment, the change being made to ensure the proper understanding that the composition should comprise at least some ethanol.

Dependent claims (which are multiple dependent claims) have been amended to also depend from various of the new independent claims 61-64.

Entry and consideration of the claim amendments is respectfully requested.

New Claims

New claims 61-64 have been added. Support for new claim 61 may be found in pending claim 32, noting that new claim 61 is without a recitation directed to the solution comprising ethanol. Similarly, support for new claim 62 may be found in pending claim 56, noting that new claim 62 is without a recitation directed to the solution comprising ethanol. And, support for new claim 63 may be found in pending claim 57, noting that new claim 63 is without a recitation directed to the solution comprising ethanol. Support for new claim 64 may be found in canceled claim 55.

New claims 61-64 are patentable over the cited art at least for reasons detailed herein.

Entry and consideration of the new claims is respectfully requested.

Art Rejections - Fahim + Wider

Claims 32, 34, 39, 41, 42, 45 and 56-60 stand rejected under 35 USC § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (USPN 6,500,861). Applicants traverse the rejection for at least the reasons discussed below. However, applicants make no admissions from a lack of a response to any of the Office's assertions.

This application has been appealed to the Board of Patent Appeals and Interferences ("Board") wherein the Board affirmed the rejection of certain claims based on Fahim in view of Wider. The Board made this decision based on the evidence in front of it. However, Applicants now offer new evidence, in the form of declarations and publications, which materially affect the basis for the Board's decision. Accordingly, the Examiner is requested to fully consider the rejection of the pending claims in view of all the evidence now of record.

Further, the Examiner rejected the then-pending claims, asserting that Fahim teaches the presence of ethanol. Applicants respectfully traverse this assertion.

1 - Fahim Does Not Teach The Presence of Ethanol

Exemplary claim 32 recites that the solution further comprises between 0% and 10% (v/v) ethanol and water.

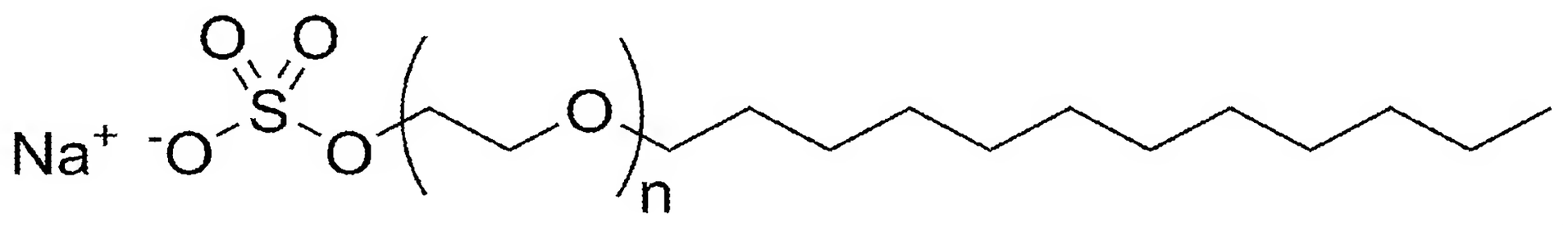
The Examiner asserts that:

> the antimicrobial compositions taught by Fahim comprise ethanol. See page 16, lines 3-6, Table 1, Table 2, table 8, wherein it is taught that 8 weight percent of sulfotext, sodium lauryl ether sulfate employed in the compositions there contains about 13-16 % of ethanol i.e. less than 10 % (v/v) of ethanol is present in the compositions therein.

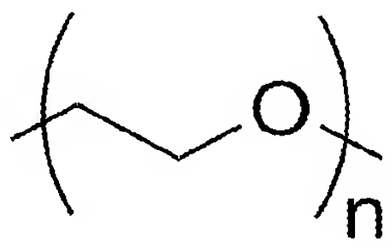
Official Action mailed 08/04/2009, page 3.

Specifically, Fahim discloses "Sodium lauryl ether sulfate contains about 13-16% ethanol which helps dissolve PCMX and triclosan along with propylene glycol." Fahim, page 16, lines 5-6.

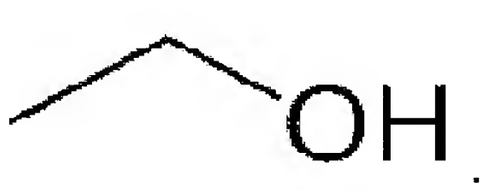
While applicants understand how the Examiner was misled by the disclosure of Fahim, it is clear to one skilled in the art that a solution with sodium lauryl ether sulfate ("SLES") does not actually comprise any ethanol. The chemical formula of SLES is as follows:



And, the "ethanol" referred to by Fahim is actually the repeating unit (shown below) in the middle of the chain of the SLES:



As one skilled in the art readily recognizes, ethanol is of the following formula:



A repeating unit, in the middle of a chain, that is somewhat structurally similar to ethanol is not a teaching of ethanol as a separate chemical entity. Accordingly, there is not actually any ethanol in the solution of Fahim. However, exemplary claim 32 recites that the solution further comprises between 0% and 10% (v/v) ethanol and water. Therefore the Examiner has not presented a proper *prima facie* finding of obviousness.

2 - The Solution Of Fahim Is Toxic

The Examiner has asserted that:

> It would have been obvious to a person in ordinary skill in the art to employ the antimicrobial composition of Fahim in a sterile pyrogen free condition because Wider teaches antimicrobial compositions as packaged in a sterile and pyrogen free form.
>
> One of ordinary skill in the art at the time of the invention would have been motivated to employ the claimed antiseptic compositions in a sterile pyrogen free form as conventional with antimicrobial compositions with the expectation of using the composition in catheters.

Official Action mailed 08/04/2009, page 4.

However, the Examiner is respectfully requested to reconsider this assertion is view of the new evidence Applicants present herewith.

The handwash of Fahim comprises at least the following antimicrobial components:

- Triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether);
- PCMX (4-chloro-3,5-dimethyl phenol); and
- Glutaraldehyde.

Fahim, pages 8, line 9 to page 9, line 9.

However, such a handwash would be toxic to the skin of a user, and would be particularly toxic in the bloodstream of a user. See Declaration of Olmstead & Ketteridge, paragraphs 3-11.

Since the handwash of Fahim is toxic, one skilled in the art would have no reason to make the hand wash of Fahim sterile and non-pyrogenic.

For example, since the handwash of Fahim is toxic, the handwash is not actually useful on the skin of a user. Because the handwash of Fahim is not useful

on the skin of a user, one skilled in the art would not modify such handwash based on the teachings of Wider, which is a non-toxic substance which may be applied to the skin and internally. One skilled in the art would only possibly have reason to apply the teachings of Wider to a substance that is actually useful on the skin and internally. However, one skilled in the art would not apply the teachings of Wider to a toxic substance that is not useful on the skin of a user.

And, beyond exposure to the skin, one skilled in the art would have clear reason not to employ the toxic Fahim composition in a sterile pyrogen free form with the expectation of using the Fahim composition in catheters. Catheters are used intimately with a patient's body and allow the contents thereof potential contact with a patient's bloodstream or to otherwise be possibly introduced into a patient's body. Thus, one skilled in the art would not to employ the toxic Fahim composition in a sterile pyrogen free form with the expectation of using the Fahim composition in catheters, as asserted by the Office ("One of ordinary skill in the art at the time of invention would have been motivated to employ the claimed antimicrobial compositions in a sterile pyrogen free form as conventional with antimicorbial compositions with the expectation of using the compositions in catheters." Official Action mailed 08/04/2009, page 4.)

As the Declaration of Olmstead & Ketteridge evidences, the handwash of Fahim contains the highly toxic compound glutaraldehyde, a component that the FDA has not approved for inclusion in antibacterial hand soap. Declaration of Olmstead & Ketteridge, paragraphs 7-11.

Moreover, use of the handwash of Fahim would involve exposure to glutaraldehyde which causes the following health effects: throat or lung irritation; asthma and difficulty breathing; contact and/or allergic dermatitis; nasal irritation;

sneezing; wheezing; burning eyes and conjunctivitis. Declaration of Olmstead & Ketteridge, paragraph 8.

Glutaraldehyde is shown to have an LD_{50}[1] (intravenous) in a rat of just 9.8 mg/kg and when administered orally to rats the LD50 is 134 mg/Kg. Declaration of Olmstead & Ketteridge, paragraph 9. Further, to demonstrate the toxicity of the Fahim handwash, only about 4 mL of a water solution with the same amount of glutaraldehyde that Fahim used in Examples 1-9 is required to kill an average rat. Declaration of Olmstead & Ketteridge, paragraph 11. A substance is considered highly toxic when the LD_{50} is more than 50 milligrams per kilogram but not more than 500 mg/Kg of body weight when administered orally to albino rats. Declaration of Olmstead & Ketteridge, paragraph 10.

Glutaraldehyde is therefore a highly toxic substance. Declaration of Olmstead & Ketteridge, paragraph 10. When ingested or given parenterally, ***glutaraldehyde is a poison***. Declaration of Olmstead & Ketteridge, paragraph 10.

Thus, the Office can not assert that one skilled in the art would modify the toxic, poisonous handwash of Fahim for use in a catheter, with potential introduction with a patient's bloodstream.

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[1] LD_{50} (abbreviation for "Lethal Dose, 50%") is the median lethal dose of a toxic substance required to kill half the members of a tested population. LD_{50} figures are frequently used as a general indicator of a substance's acute toxicity. The LD_{50} is usually expressed as the mass of substance administered per unit mass of test subject, such as grams of substance per kilogram of body mass. Stating it this way allows the relative toxicity of different substances to be compared, and normalizes for the variation in the size of the animals exposed (although toxicity does not always scale simply with body mass). Typically, the LD_{50} of a substance is given in milligrams per kilogram of body weight. Declaration of Olmstead & Ketteridge, paragraph 9.

The handwash of Fahim also contains 4-chloro-3,5-dimethyl phenol (Chloroxylenol, also known as parachlorometaxylenol, or PCMX) as a component. While PCMX is used as an antimicrobial in soaps, shampoos, and sprays, it has never been approved for oral or parenteral administration. Declaration of Olmstead & Ketteridge, paragraph 5. Despite its topical use, PCMX may be a skin, eye or respiratory tract irritant and is considered harmful if swallowed. Declaration of Olmstead & Ketteridge, paragraph 5. PCMX is highly corrosive and causes caustic eye, skin, mouth and gastrointestinal injuries. Ingestion can result in nausea, vomiting, diarrhea, hypotension, myocardial failure, pulmonary edema, neurological changes, liver and renal toxicity, methemoglobinemia, and hemolysis. Declaration of Olmstead & Ketteridge, paragraph 5. It is readily apparent that this component of Fahim cannot be sterilized, placed in a vial, and administered to humans. Declaration of Olmstead & Ketteridge, paragraph 5. According to Dr. Olmstead and Pharmacist Ketteridge, no reasonable practitioner skilled or even unskilled in the art would even think about doing this. Declaration of Olmstead & Ketteridge, paragraph 5.

Moreover, PCMX in the Fahim handwash is shown to have an LD_{50} (oral injection) for a mouse of 1,000 mg/kg and an LD_{50} (oral injection) for a rat of 3830 mg/kg. Declaration of Olmstead & Ketteridge, paragraph 6.

And, triclosan in the Fahim handwash has been questioned in regard to environmental and human health. Declaration of Olmstead & Ketteridge, paragraph 4. The United States Environmental Protection Agency (EPA) has registered it as a pesticide and gives triclosan high scores as a human health risk. Declaration of Olmstead & Ketteridge, paragraph 4. The molecular structure of this compound is similar to some of the more toxic chemicals such as dioxins and PCBs. Declaration

of Olmstead & Ketteridge, paragraph 4. Triclosan is a chlorophenol, a class of chemicals suspected of causing cancer in humans, and was the subject of a United Kingdom cancer alert. Declaration of Olmstead & Ketteridge, paragraph 4. Externally, chlorophenol can cause a variety of skin irritations, but since they can temporarily deactivate sensory nerve endings, contact with it may cause little or no pain. Declaration of Olmstead & Ketteridge, paragraph 4. Taken internally, even in small amounts, chlorophenol can lead to cold sweats, circulatory collapse, convulsions, coma, and death. Declaration of Olmstead & Ketteridge, paragraph 4.

Clearly, due to the toxicity of the handwash of Fahim, one skilled in the art would not employ the Fahim compositions in catheters. Because one skilled in the art would not employ the Fahim compositions in catheters, one skilled in the art would have no reason to modify the handwash to be in a sterile pyrogen free form with the expectation of using the Fahim composition in catheters.

As demonstrated above, one skilled in the art would have no reason to make the handwash composition of Fahim sterile and non-pyrogenic. The handwash composition of Fahim is toxic and would not be used in the manner of Wider. The toxic composition of Fahim would not be used in a catheter or on skin.

Applicants respectfully asserts that in light of the new information regarding the toxicity of the Fahim composition there is no reason one skilled in the art would have made the alleged modification of Fahim.

Accordingly, based on the new evidence presented to the Office, applicants respectfully submit that the present obviousness rejection cannot be sustained. There must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *KSR v. Teleflex,* 82 USPQ2d 1385, 1396 (2007). However, at least as demonstrated by the information in the

Declaration of Olmstead & Ketteridge, there can be no articulated reasoning for one skilled in the art to modify the toxic handwash of Fahim as asserted by the Office.

In addition to having no reason to make the asserted modification, applicants respectfully assert that there are specific reasons *not* to make the asserted modification.

First, the handwash of Fahim cannot be sterilized by the method of Wider, heat. Declaration of Olmstead & Ketteridge, paragraph 14. Triclosan is heat stable only up to 482ºF (250ºC), but it readily decomposes into dioxins. Declaration of Olmstead & Ketteridge, paragraph 14. Dioxins are a poison that accumulates in the body and contributes to cancer, liver damage and an elevated risk of diabetes. Declaration of Olmstead & Ketteridge, paragraph 14. Glutaldehyde is volatile and cannot withstand temperatures required for sterilization. Declaration of Olmstead & Ketteridge, paragraph 14. Each of the embodiments of Fahim's teachings contain propylene glycol and any solution containing propylene glycol in a container will explode on heating. Declaration of Olmstead & Ketteridge, paragraph 14.

And, the handwash of Fahim cannot be sterilized by filtration. Declaration of Olmstead & Ketteridge, paragraph 16. The viscosity of the Fahim hand soap compositions are in the range of 780 to 900 centipoise (cps). Declaration of Olmstead & Ketteridge, paragraph 16. As a reference, the viscosity of water is 1 cps while the viscosity of SAE 40 motor oil is 650 to 900 cps. Declaration of Olmstead & Ketteridge, paragraph 16. The Fahim soaps are as viscous and thick as motor oil. Declaration of Olmstead & Ketteridge, paragraph 16. This would preclude filtration for sterilization. Declaration of Olmstead & Ketteridge, paragraph 14. It is not only *not* obvious to sterilize the Fahim compositions, it is not possible to do so.

Declaration of Olmstead & Ketteridge, paragraph 14. Accordingly, no one skilled in the art would think to do so.

Thus, there is no safe and acceptable method to sterilize the solution of Fahim.

Wider teaches that USP grade ingredients are used to obtain a sterile and pyrogen free solution in order to receive US Food and Drug administration marketing approval to allow for use in humans. See, e.g., Wider, column 7, lines 35-52. USP refers to the United States Pharmacopeia, an official public standards–setting authority for all prescription and over–the–counter medicines and other health care products manufactured or sold in the United States. Declaration of Olmstead & Ketteridge, paragraph 15.

However, even if sterile, pyrogen-free, deionized water (as used in Wider) were used with the Fahim composition, the final product would be very difficult to render pyrogen free since none of the other ingredients are ready available with a specification of low or no pyrogens. Declaration of Olmstead & Ketteridge, paragraph 15. Pyrogens are very difficult and expensive to remove from a final formulation, and the acceptable production method to assure no pyrogens in a final formulation is to only utilize ingredients containing no pyrogens. Declaration of Olmstead & Ketteridge, paragraph 15. Typically, ingredients intended for injection into the body are available in a pyrogen free presentation. Declaration of Olmstead & Ketteridge, paragraph 15. However, since the discussed ingredients contained in the Fahim formulations are never used in products intended to be injected or otherwise contact the systemic circulation, they are not available with a specification of pyrogen free. Declaration of Olmstead & Ketteridge, paragraph 15. Thus, without

non-pyrogenic starting materials (besides the water), the handwash of Fahim will not be non-pyrogenic.

Thus, while applicants maintain there is no reason to provide the toxic composition of Fahim in a sterile and non-pyrogenic form, applicants also maintain that, even with some reason, one skilled in the art would not do such. That is, without non-pyrogenic components and without a safe and acceptable method to sterilize the solution of Fahim, one skilled in the art would not modify the toxic composition of Fahim to be in a sterile and non-pyrogenic form.

Claim 56

With regard to claim 56, the Office asserts that:

> the [alleged] intended use of the composition "wherein the lock flush composition is biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes", does not further limit the claim because the recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Official Action mailed 08/04/2009, page 4.

That is, the Office is asserting that the handwash of Fahim is biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes. Biocompatible is defined as follows "the condition of being compatible with living tissue or a living system by not being toxic or injurious and not causing immunological rejection." *Merriam-Webster's Medical Dictionary*, 2002.

Based on the evidence presented above with the Declaration of Olmstead & Ketteridge, the handwash of Fahim is not biocompatible. The Fahim handwash is toxic and injurious to living tissue and living systems. Thus, there is a structural difference between the claimed invention and Fahim that patentably distinguishes the claimed invention from Fahim.

Art Rejections - Fahim + Wider + Root

Claim 47 stands rejected under 35 USC § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (USPN 6,500,861) and further in view of Root. Applicants traverse the rejection for at least the reasons discussed below. However, applicants make no admissions from a lack of a response to any of the Office's assertions.

Art Rejections - Fahim + Wider + Remington's

Claim 46 stands rejected under 35 USC § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (USPN 6,500,861) and further in view of Remington's Pharmaceutical Sciences. Applicants traverse the rejection for at least the reasons discussed above. However, applicants make no admissions from a lack of a response to any of the Office's assertions.

Conclusion

If there are any questions concerning this response, or the application in general, the Examiner is respectfully requested to telephone the undersigned attorney at the number provided below.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.20(d) and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

Date: 2 February 2010

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